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High Production Volume (HPV) Challenge Program Test Plan and Data Review

Dinonylnaphthalene Category

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Acronyms and Abbreviations

EPA	U.S. Environmental Protection Agency
EPI	estimations programs interface
EQC	Equilibrium Criterion model
HPV	High Production Volume Challenge Program
Kow	octanol-water partition coefficient
OECD	Organisation for Economic Cooperation and Development
SAR	structure activity relationship
SIDS	Screening Information Data Set

Executive Summary

King Industries committed to sponsoring four chemicals as part of the U.S. Environmental Protection Agency's (EPA) High Production Volume (HPV) Challenge Program. These chemicals include diisononylnaphthalene (CAS No. 63512-64-1); dinonylnaphthalene sulfonic acid (CAS No. 25322-17-2); dinonylnaphthalene sulfonic acid, calcium salt (CAS No. 57855-77-3); and dinonylnaphthalene sulfonic acid, barium salt (CAS No. 25619-56-1). As part of King Industries' commitment, Exponent has assembled available data and prepared a test plan to develop additional screening level data on human health effects, environmental fate and effects, and physicochemical properties for the dinonylnaphthalene category. This category was developed based on the similar physicochemical and toxicological properties of the sponsored chemicals. As recommended in EPA guidance, the intent of the test plan is to maximize the use of existing and scientifically adequate data to minimize animal testing.

Introduction

This document provides an overview of the data available for the Screening Information Data Set (SIDS) endpoints for the members of the dinonylnaphthalene category. The SIDS battery includes acute toxicity, repeated dose (or subchronic) toxicity, developmental/reproductive toxicity, mutagenicity, ecotoxicity, environmental fate, and physicochemical properties (OECD 1997). The members of the dinonylnaphthalene category that will be discussed in this test plan are summarized in Table 1.

Table 1. CAS Numbers and Descriptions of Dinonylnaphthalene Category Members

CAS Number	**CAS Number Description**
63512-64-1	Diisononylnaphthalene (a.k.a. dinonylnaphthalene)
25322-17-2	Dinonylnaphthalene sulfonic acid
25619-56-1	Dinonylnaphthalene sulfonic acid, barium salt
57855-77-3	Dinonylnaphthalene sulfonic acid, calcium salt

In preparing the test plan, we reviewed data from the company's proprietary files and/or calculated endpoints using the widely accepted structure activity relationship (SAR) Equilibrium Criterion model (EQC; Mackay et al 1996; Canadian Environmental Modelling Centre 2003) and EPI Suite™ package (EPA 2000).

Description of the Dinonylnaphthalene Category

In the HPV guidance, the EPA included a provision for the use of SAR to reduce testing needs (EPA 1999a). In the guidance, a chemical category is "a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity (EPA 1999b). The goal of developing a chemical category is to use interpolation and/or extrapolation to assess chemicals rather than conducting additional testing.

The four chemicals discussed in this test plan are part of the dinonylnaphthalene category and have similar functional groups and physical and chemical properties. All of the chemicals are based on the dinonylnaphthalene moeity (Figure 1). Diisononylnaphthalene (also known as dinonylnaphthalene) is a closed system intermediate that is produced by the controlled alkylation of naphthalene with nonene. It is the starting material for all of the other members of this category.

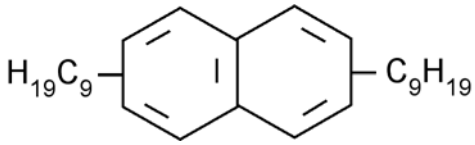

Figure 1. Chemical structure of dinonylnaphthalene

Dinonylnaphthalene sulfonic acid is produced by the subsequent sulfonation of diisononylnaphthalene. The barium and calcium salts are produced by direct neutralization of the dinonylnaphthalene sulfonic acid. These chemicals, with the exception of diisononylnaphthalene, are used as additives in industrial lubricants, greases, metalworking fluids, industrial coatings, and rust preventives. They are generally supplied, as 50% active, to industrial formulators who add them into their formulated products at typical concentrations ranging from 0.5 to 3 weight percent.

The physical and chemical properties of the members of the dinonylnaphthalene category are similar. The members of this category are dark-colored viscous liquids (as supplied) that are used as additives in industrial formulations, and are not intended to be used as stand-alone chemicals. They are stable at temperatures greater than 100 ºC, have low volatilities and vapor pressures, high viscosities, and are poorly soluble in water. The most likely route of human exposure is skin and eye contact of workers involved in manufacture, blending, transport, and disposal. Inhalation of these chemicals is likely to be low due to their low vapor pressure and high viscosity. The most likely source of environmental exposure is accidental spills at manufacturing sites and during transport.

Matrix of SIDS Endpoints

The strategy for the dinonylnaphthalene category was to evaluate data on the likely most reactive member based on available physicochemical modeling and acute toxicity results. Each available study on category members was evaluated for adequacy, and robust summaries were prepared (Appendix A). A matrix of SIDS endpoints for the members of the dinonylnaphthalene category is presented in Table 2.

Table 2. Matrix of Available and Adequate Data for Dinonylnaphthalene Category

Test	Diisononylnaphthalene	Dinonylnaphthalene sulfonic acid	Dinonylnaphthalene sulfonic acid, calcium salt	Dinonylnaphthalene sulfonic acid, barium salt
Physicochemical Properties				
Melting Point	CM	CM	CM	CM
Boiling Point	CM	CM	CM	CM
Vapor Pressure	CM	CM	CM	CM
Partition Coefficient	CM	CM	CM	CM
Water Solubility	CM	CM	CM	CM
Environmental Fate				
Photodegradation	NA	NA	NA	NA
Stability in Water (Hydrolysis)	NA	NA	NA	NA
Transport/Distribution	CM	CM	CM	CM
Biodegradation	---	Test	---	---
Ecotoxicity				
Acute Toxicity to Fish	---	Test	---	---
Acute Toxicity to Aquatic Invertebrates (Daphnia)	---	Test	---	---
Acute Toxicity to Aquatic Plants (Algae)	---	Test	---	---
Toxicity				
Acute Toxicity (Oral)	A	A	A	A
Acute Toxicity (Inhalation)	A	A	A	A
Acute Toxicity (Dermal)	A	A	A	A
Repeated Dose Toxicity	---	---	---	Test
Skin Irritation/ Corrosion	A	A	A	A
Eye Irritation	A	A	A	A
Sensitization	---	---	A	A
Genetic Toxicity – Gene Mutation	---	---	---	Test
Genetic Toxicity – Chromosomal Aberration	---	---	---	Test
Reproductive Toxicity	---	---	---	TBD
Developmental Toxicity	---	---	---	TBD

A = Study data are available and considered adequate.
CM = Data requirement fulfilled based on computer modeling.
NA = Endpoint not applicable due to physical/chemical properties of chemical.
---- = No data available.
Test = Endpoint for category to be fulfilled with testing; read-across to remaining members of category.
TBD = Need for testing to be determined following completion of the repeated dose toxicity study.

Assessment of Data Quality and Availability

Physicochemical Properties

Physicochemical data for each of the members of the dinonylnaphthalene category are summarized in Table 3. These data were developed using the EQC model and EPI Suite™ package (Mackay et al 1996; Canadian Environmental Modelling Centre 2003; EPA 2000). Boiling points for the chemicals ranged from 452.3 to 1124.1 ºC and melting points ranged from 168.4 to 349.8 ºC. Vapor pressures for all of the chemicals were very low, and ranged from $1.4x10^{-8}$ to $4.8x10^{-29}$ mm Hg. All of the members of the dinonylnaphthalene category are poorly soluble in water, with solubility ranging from $2.8x10^{-5}$ to $1.0x10^{-10}$ mg/L. The octanol-water partition coefficients (Kows) for the chemicals are very high, with values for the log Kows ranging from 9.0 to 23.3. All of the physicochemical endpoints required as part of the SIDS battery are fulfilled using data calculated by the SAR models. As a result, no additional physicochemical testing is proposed for this program.

Table 3. Summary of Modeled Physicochemical Results for Members of the Dinonylnaphthalene Category

Parameter	Diisononylnaphthalene	Dinonylnaphthalene sulfonic acid	Dinonylnaphthalene sulfonic acid, calcium salt	Dinonylnaphthalene sulfonic acid, barium salt
Melting point (ºC)	168.4	259.5	261.5	349.8
Boiling point (ºC)	452.3	600.4	604.7	1124.1
Vapor pressure (mm Hg)	1.4×10^{-8}	3.9×10^{-16}	1.4×10^{-13}	4.8×10^{-29}
Water solubility (mg/L)	2.4×10^{-7}	2.8×10^{-5}	3.1×10^{-7}	1.0×10^{-10}
log Kow	11.97	9.0	10.96	23.3

Environmental Fate

Environmental fate, transport, and distribution evaluations were conducted using the EPI Suite™ package (EPA 2000) for all members of the dinonylnaphthalene category. Based on the results of the Level I, II, and III fugacity simulations, all of the chemicals are predicted to partition in the environment primarily to soil and sediment, with minimal partitioning to air or water.

Advective losses and intermedia exchange of materials between environmental compartments were determined to be insignificant in the simulations.

The EPI Suite™ package (EPA 2000) was unable to estimate the potential atmospheric oxidation potential for members of the dinonylnaphthalene category based on their chemical structure. However, these chemicals are not expected to partition into air, so photodegradation can be considered an irrelevant process for this category. Additionally, the members of the dinonylnaphthalene category are predicted to be resistant to hydrolysis since they lack potentially hydrolysable groups such as alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Lyman et al. 1982, Neely 1985).

Based on their chemical structure, members of the dinonylnaphthalene category are expected to degrade very slowly in the environment. An OECD 301 study (Ready Biodegradability) will be completed on dinonylnaphthalene sulfonic acid. Dinonylnaphthalene sulfonic acid was chosen for the biodegradation study since it expected to be the most reactive in water and possesses the highest predicted water solubility. Results from the biodegradation study will be used to read across to other members of the category for the biodegradation end point. The recommended testing, together with the existing modeled data, will be sufficient to adequately characterize the environmental fate of the chemicals included in the dinonylnaphthalene category.

Ecotoxicity

Due to their low water solubility, members of the dinonylnaphthalene category are not expected to be toxic to aquatic organisms. Acute limit tests (single exposure concentration of 1,000 mg/L) with rainbow trout (OECD 203, Fish Acute Toxicity Test), *Daphnia magna* (OECD 202, Daphnia sp. Acute Immobilization Test) and *Selenastrum capricornutum* (OECD 201, Alga Growth Inhibition Test) will be conducted with dinonylnaphthalene sulfonic acid in accordance with the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (OECD 2000). Dinonylnaphthalene sulfonic acid was chosen for the aquatic studies since it expected to be the most reactive in water and is predicted to have the highest water solubility. Limit tests (single exposure concentration of 1,000 mg/L) were chosen since the

members of the dinonylnaphthalene category are not expected to partition into water to any great extent based on their low predicted water solubility. If aquatic effects are seen during the limit test, a definitive toxicity test will be conducted with that test organism. Results from the studies with dinonylnaphthalene sulfonic acid will be used to read across to other members of the category for the ecotoxicity end points.

Toxicity

Acute oral, inhalation, and dermal toxicity studies are available for each of the members of the dinonylnaphthalene category (Table 4). The chemicals exhibit a very low order of toxicity to rats or rabbits by the oral, inhalation, or dermal routes. Study results for skin and eye irritation are available for category members, even though these endpoints are not part of the SIDS battery. Human sensitization study results (additional non-SIDS studies) are also available for two members of the category (dinonylnaphthalene sulfonic acid, calcium salt; dinonylnaphthalene sulfonic acid, barium salt). Based on the available toxicity results, dinonylnaphthalene sulfonic acid, barium salt appears to be the most biologically active member of the category.

Table 4. Summary of Toxicity Results for Members of the Dinonylnaphthalene Category

Parameter	**Diisononylnaphthalene**	**Dinonylnaphthalene sulfonic acid**	**Dinonylnaphthalene sulfonic acid, calcium salt**	**Dinonylnaphthalene sulfonic acid, barium salt**
Acute Toxicity Oral (mg/kg)	>5,000	>5,000	>5,000	3.5 ml/kg (gavage) >5,000 (food)
Acute Toxicity Inhalation (mg/L)	>17	>200	>18	>21
Acute Toxicity Dermal (g/kg)	>20	>2	>20	>2 mL/kg
Skin Irritation /Corrosion	Mild irritant Non-corrosive	Moderate irritant	Moderate irritant Non-corrosive	Moderate irritant Non-corrosive
Eye Irritation	Mild irritant	Severe irritant	Irritant	Severe irritant (diluent oil) Minimal irritant (corn oil) Irritant (Light mineral oil)
Sensitization	-----	-----	Non-sensitizer (human)	Non-sensitizer (human)

A combined repeated dose rat oral (gavage) toxicity study with the reproduction/developmental toxicity screening study (OECD 422) will be completed on dinonylnaphthalene sulfonic acid, barium salt. The oral route of exposure was chosen for the health effects testing, since it is likely to be the most sensitive route of exposure based on the acute toxicity results and since limited absorption via the dermal and inhalation routes is anticipated for these chemicals due to their low solubility, high viscosity, and low vapor pressure. The need for additional testing, including conduct of developmental and/or reproductive studies, will be determined after evaluation of the results from the repeated dose study.

Mutagenicity studies including a bacterial reverse mutation test (OECD 471) and an *in vitro* mammalian chromosomal aberration test (OECD 473) will also be conducted on dinonylnaphthalene sulfonic acid, barium salt. Results from these studies will be used to read across to other members of the category. The recommended testing, together with the existing acute toxicity data, will be sufficient to adequately characterize the toxicity of the members of the dinonylnaphthalene category.

Test Plan Summary

As outlined in the sections discussed above, the following testing will be conducted for the dinonylnaphthalene category:

- Biodegradation test (OECD 301) with dinonylnaphthalene sulfonic acid
- Acute fish limit test (OECD 203) with dinonylnaphthalene sulfonic acid
- Acute Daphnia limit test (OECD 202) with dinonylnaphthalene sulfonic acid
- Acute alga limit test (OECD 201) with dinonylnaphthalene sulfonic acid
- Repeated dose toxicity test with the reproduction/developmental screening test (OECD 422) with dinonylnaphthalene sulfonic acid, barium salt
- Bacterial reverse mutation test (OECD 471) with dinonylnaphthalene sulfonic acid, barium salt
- Mammalian chromosomal aberration test (OECD 473) with dinonylnaphthalene sulfonic acid, barium salt

Based on computer modeling and company proprietary data, the physicochemical endpoints are fulfilled by available data. No additional testing is proposed for this category. No acute mammalian toxicity studies are proposed as well, since sufficient data are available to fulfill the acute toxicity endpoints.

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